Persistent Brain Injury in HIV Patients on ART

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Background: Numerous studies reported CNS damage due to HIV prior to anti-retroviral therapy (ART). Antiviral medications are now in widespread use, greatly mediating the immune suppressing effects of HIV, but ART may not halt CNS damage. The goal of this project was to determine the effects of HIV on the brain of participants, most of whom have been on effective ART.

Methods: Seventy-one (71) HIV^+ subjects (44 ±8yrs, log viral load = 8.89 ±2.38, Sqrt CD4 = 18.55 ±5.36, CDC Class: 39% A, 20% B, 14% on no medication, 25% on 1–2 ART medications, 61% on 3 or more ART medications), and 75 controls (41 ±9yrs) were carefully screened for other CNS disease and studied with: 1) structural MRI, to measure volumes of gray matter (GM) and white matter (WM) in each lobe and other brain structures, and to perform deformation morphometry to quantify shape differences between all brain structures without a priori definition of regions-of-interest; 2) MR perfusion, yielding absolute blood flow measurements in lobar GM and WM; 3) MR spectroscopic imaging (MRSI), for choline (Cho, a measure of inflammation) concentrations in GM and WM in each lobe; 4) neuropsychological (NP) testing, yielding summary scores in major cognitive domains; and 5) EEG-event related potentials (ERP), to measure P3a, P3b, and CNV amplitude and latencies.

Results: We found significant (t-statistic, $p < 0.05$) differences in these measures between the HIV^+ and HIV^- groups. HIV^+ participants had: 1) lower GM volumes throughout the brain, contractions of tissue in GM, WM, and thalamus, and CSF expansions detected by deformation morphometry (figure); 2) lower frontal GM blood flow; 3) higher parietal WM Cho; 4) impaired working memory, processing speed, and global cognition; and 5) prolonged latency of the auditory and visual P3b, reduced amplitude of auditory P3b, and late phase of the contingent negative variation (CNV). Finally, preliminary longitudinal studies on 32 HIV^+ and

16 HIV^- participants (mean scan interval 26 mos) show progressing brain tissue loss and cognitive deterioration.

Conclusions: HIV^+ subjects on “effective” ART have widespread GM volume loss, WM contractions, parietal WM inflammation, and impaired cognition as measured by NP testing and ERPs. Preliminary longitudinal results suggest that HIV mediated brain injury is an ongoing process despite ART.